Claims

What is claimed is:

1. A method for identifying a specific amino acid residue dependent antibody to a target protein or peptide, which method comprises:

a) providing an antibody that binds to a target protein or peptide containing a specific amino acid residue;

b) contacting said antibody provided in step a) with a negative screening protein or peptide comprising said target protein or peptide wherein said specific amino acid residue is lacking or unavailable for binding with said antibody; and

c) assessing binding between said antibody and said target protein or peptide and assessing binding between said antibody and said negative screening protein or peptide, whereby identifying an antibody that binds to said target protein or peptide, but fails to bind to said negative screening protein or peptide, as a specific amino acid residue dependent antibody.

2. The method of claim 1, wherein the antibody that binds to a target protein or peptide is provided by immunizing a mammal with an immunizing protein or peptide comprising said target protein or peptide or an immunizing nucleic acid encoding a protein or peptide comprising said target protein or peptide.

3. The method of claim 2, wherein the immunizing protein or peptide comprises more amino acid residue(s) than the target protein or peptide and the immunizing nucleic acid encodes a protein or peptide that comprises more amino acid residue(s) than the target protein or peptide.

4. The method of claim 2, wherein the immunizing protein or peptide is the target protein or peptide and the immunizing nucleic acid encodes the target protein or peptide.

5. The method of claim 1, wherein the antibody that binds to a target protein or peptide is provided by identifying an antibody that is known to bind to the target protein or peptide.

6. The method of claim 1, wherein the antibody binds to a target protein or peptide specifically.

7. The method of claim 1, wherein the target protein or peptide is a marker of parathyroid gland disease status, renal bone disease, osteoporosis, bone turnover status, the extent of partial or complete parathyroid gland removal.

8. The method of claim 1, wherein the target protein or peptide is PTH, or a fragment thereof.

9. The method of claim 1, wherein the negative screening protein or peptide lacks one, two, three, four, five, six, seven, eight, nine, ten or more than ten amino acid residues from the target protein or peptide.

10. The method of claim 1, wherein the identified amino acid residue dependent antibody depends on one specific amino acid residue of the target protein or peptide.

11. The method of claim 1, wherein the identified amino acid residue dependent antibody depends on two or more specific amino acid residues of the target protein or peptide.

12. A specific amino acid residue dependent antibody, which specific amino acid residue dependent antibody is produced by the method of claim 2.

13. The method of claim 1, further comprising attaching the identified specific amino acid residue dependent antibody to a surface of a solid phase device suitable for testing for a target protein or peptide.

14. The method of claim 1, further comprising attaching the identified specific amino acid residue dependent antibody to a label.

15. A specific amino acid residue dependent antibody suitable for testing for a target protein or peptide, which specific amino acid residue dependent antibody is produced by the method of claim 1.

16. A device suitable for testing for a target protein or peptide, which device is produced by the method of claim 13.

17. A method for producing a specific amino acid residue dependent antibody to a target protein or peptide, which method comprises:

a) providing an antibody mixture wherein at least one of said antibodies in said mixture binds to a target protein or peptide containing a specific amino acid residue;

b) contacting said antibody mixture provided in step a) with a negative screening protein or peptide comprising said target protein or peptide wherein said specific amino acid residue is lacking or unavailable for binding with said antibody;

c) removing from said mixture an undesired antibody that binds to said negative screening protein or peptide; and

d) recovering from said mixture a desired antibody that binds to said target protein or peptide but fails to bind to said negative screening protein or peptide as a specific amino acid residue dependent antibody.

18. The method of claim 17, wherein the negative screening protein or peptide is attached to a solid phase.

19. The method of claim 18, wherein the solid phase can be separated from the antibody mixture to remove undesired antibodies that bind to the negative screening protein or peptide.

20. The method of claim 17, wherein the antibody mixture is passed through a column comprising the negative screening protein or peptide affixed to a solid phase to retain an undesired antibody that binds to the negative screening protein or peptide in the column while allowing a desired antibody that does not bind to the negative screening protein or peptide to pass through.

21. The method of claim 17, further comprising a positive screen to collect the desired antibodies.

22. The method of claim 17, further comprising attaching the produced specific amino acid residue dependent antibody to a surface of a solid phase device suitable for testing for a target protein or peptide.

23. The method of claim 17, further comprising attaching the produced specific amino acid residue dependent antibody to a label.

24. A specific amino acid residue dependent antibody suitable for testing for a target protein or peptide, which specific amino acid residue dependent antibody is produced by the method of claim 17.

25. A device suitable for testing for a target protein or peptide, which device is produced by the method of claim 22.

26. A method of testing for a target protein or peptide in a sample, which method comprises:

a) contacting a sample containing or suspected of containing a target protein or peptide with a specific amino acid residue dependent antibody under suitable conditions to allow binding of said target protein or peptide, if present in said sample, to said specific amino acid residue dependent antibody, wherein said specific amino acid residue dependent antibody is capable of binding to said target protein or peptide but is incapable of binding to a protein or peptide comprising said target protein or peptide wherein said specific amino acid residue is lacking or unavailable for binding with said antibody; and

b) assessing binding between said target protein or peptide with said specific amino acid residue dependent antibody to determine the presence and/or amount of said target protein or peptide in said sample.

27. The method of claim 26, wherein the specific amino acid residue dependent antibody is identified by a method comprising:

a) providing an antibody that binds to a target protein or peptide containing a specific amino acid residue;

b) contacting said antibody provided in step a) with a negative screening protein or peptide comprising said target protein or peptide wherein said specific amino acid residue is lacking or unavailable for binding with said antibody; and

c) assessing binding between said antibody and said target protein or peptide and assessing binding between said antibody and said negative screening protein or peptide, whereby identifying an antibody that binds to said target protein or peptide but fails to bind to said negative screening protein or peptide as a specific amino acid residue dependent antibody.

28. The method of claim 26, wherein the specific amino acid residue dependent antibody is produced by a method comprising:

a) providing an antibody mixture wherein at least one of said antibodies in said mixture binds to a target protein or peptide containing a specific amino acid residue;

b) contacting said antibody mixture provided in step a) with a negative screening protein or peptide comprising said target protein or peptide wherein said specific amino acid residue is lacking or unavailable for binding with said antibody;

c) removing from said mixture an undesired antibody that binds to said negative screening protein or peptide; and

d) recovering from said mixture a desired antibody that binds to said target protein or peptide but fails to bind to said negative screening protein or peptide as a specific amino acid residue dependent antibody.

29. The method of claim 26, further comprising attaching the specific amino acid residue dependent antibody to a surface of a device suitable for testing for a target protein or peptide before contacting the specific amino acid residue dependent antibody with the sample.

30. The method of claim 26, further comprising attaching the identified specific amino acid residue dependent antibody to a label.

31. The method of claim 26, wherein the specific amino acid residue dependent antibody binds to the target protein or peptide specifically.

32. The method of claim 26, wherein the target protein or peptide is a marker of parathyroid gland disease status, renal bone disease, osteoporosis, bone turnover status, the extent of partial or complete parathyroid gland removal.

33. The method of claim 26, wherein the target protein or peptide is a clinical marker.

34. The method of claim 26, further comprising determining and comparing at least two of the parameters selected from the group consisting of the target protein or peptide level, the level of the negative screening protein or peptide level or a protein containing the negative screening protein or peptide, and the sum of the target protein or peptide level and the level of the negative screening protein or peptide level or a protein containing the negative screening protein or peptide.

35. The method of claim 34, wherein the comparison is in the form of a ratio, proportion, difference or product of multiplication.

36. The method of claim 34, wherein the target protein is parathyroid hormone (PTH) and the comparison is in the form of a ratio, proportion, difference or product of multiplication between unfragmented PTH and a fragment of PTH.

37. The method of claim 26, wherein the target protein or peptide is selected from the group consisting of parathyroid hormone (PTH), gastric inhibitory polypeptide (GIP), glucagon-like peptide (GLP), creatine kinase (CK), prostate specific antigen (PSA) and human chorionic gonadotropin (HCG), or a fragment thereof.

38. The method of claim 36, which is used for prognosis, diagnosis and/or treatment monitoring of familial hypocalciuria, hypercalcemia, multiple endocrine neoplasia types I and II, osteoporosis, Paget's bone disease, hyperparathyroidism, pseudohypoparathyroidism, renal failure, renal bone disease, adynamic low bone turnover renal disease, high bone turnover renal disease, osteomalacia, osteofibrosa, the extent of parathyroid gland surgical removal, oversuppression with vitamin D or a vitamin D analogue or calcium and chronic uremia.

39. The method of claim 26, wherein the specific amino acid residue dependent antibody depends on the first or first two amino acid residues of GIP and/or GLP and the method is used to distinguish among GIP and/or GLP, GIP-1 and/or GLP-1, and GIP-2 and/or GLP-2.

40. The method of claim 26, wherein the specific amino acid residue dependent antibody depends on the amino acid residues of CK located in proximity of CK isoforms (CK-MM and CK-BB and CK-MB) distinction and the method is used to distinguish CK MM from CK BB.

41. The method of claim 26, wherein the specific amino acid residue dependent antibody depends on the unique amino acid residues of HCG β subunit and the method is used to distinguish HCG from LH, TSH and FSH.

42. The method of claim 26, which is used to distinguish a modified protein or peptide from its naturally occurring counterpart, said modified protein or peptide being different from said naturally occurring counterpart by one or two amino acid residues.

43. The method of claim 42, wherein the modified protein or peptide is selected from the group consisting of insulin, calcitonin, PTH and erythropoietin.

44. A kit for testing for a target protein or peptide, which kit comprises, in a container, a specific amino acid residue dependent antibody suitable for testing for a target protein or peptide produced by the method of claim 1 and an instruction for using said specific amino acid residue dependent antibody in testing for said target protein or peptide.

45. The kit of claim 44, which further comprises a reagent(s) or means for generating a detectable signal and/or standard curve.

46. A kit for testing for a target protein or peptide, which kit comprises, in a container, a specific amino acid residue dependent antibody suitable for testing for a target protein or peptide produced by the method of claim 17 and an instruction for using said specific amino acid residue dependent antibody in testing for said target protein or peptide.

47. The kit of claim 46, which further comprises a reagent(s) or means for generating a detectable signal and/or standard curve.